FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Anesthetic and Analgesic Drug Products Advisory Committee (AADPAC) Meeting
April 19, 2023

DRAFT QUESTIONS

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1. **DISCUSSION:** Discuss the advantages and limitations of using the enriched enrollment randomized withdrawal (EERW) design to assess long-term effectiveness; discuss the advantages and limitations of using a placebo-controlled design to assess long term effectiveness.
    a) Include in your discussion the likelihood of maintaining sufficient patients in the randomized treatment period in each of these study designs to assure an adequate assessment of effectiveness at the end of the double-blind treatment period.

2. **DISCUSSION:** Discuss the proposed protocol for PMR 3033-11 (EERW). Include in your discussion the following:
    a) Is 42 to 52 weeks an adequate duration to assess the long-term effectiveness of opioids?
    b) What degree of dropout is expected in a study in this patient population? Will enough patients be expected to complete this study in order for the results to be interpretable?
    c) Is the time-to-treatment-failure endpoint informative? If yes, should use of rescue above a prespecified threshold be added as a treatment failure criterion? If no, why not?
    d) Given that the pain scores could be variable, are there measures that could be employed to assure that the threshold for increase in pain is clinically meaningful and does not represent short-term variability?
    e) Does the proposed tapering scheme adequately mitigate concerns about unblinding?
    f) Is the proposed definition of opioid-induced hyperalgesia (OIH) and surveillance for development of the condition appropriate?
    g) To better characterize, OIH, should patients diagnosed with OIH undergo a diagnostic/therapeutic opioid taper?

3. **DISCUSSION:** Discuss other designs that should be considered in the assessment of long-term effectiveness of opioids.